

WHAT IS CLAIMED IS:

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a1
1. A method of screening a test compound for its ability to inhibit or enhance the binding of angiostatin to ATP synthase comprising:

i) contacting said test compound and angiostatin with ATP synthase, or angiostatin binding portion thereof, under conditions such that angiostatin can bind to said ATP synthase, or angiostatin binding portion thereof, in the absence of said test compound, and

ii) determining the amount of angiostatin bound to said ATP synthase, or angiostatin binding portion thereof, and comparing that amount to an amount of angiostatin bound to said ATP synthase, or angiostatin binding portion thereof, in the absence of said test compound,

wherein a reduction in the amount of angiostatin bound to said ATP synthase, or angiostatin binding portion thereof, in the presence of said test compound indicates that said test compound inhibits the binding of angiostatin to said ATP synthase, or angiostatin binding portion thereof, and

wherein an increase of the amount of angiostatin bound to said ATP synthase, or angiostatin binding portion thereof, in the presence of said test compound indicates that said test compound enhances the binding of angiostatin to said ATP synthase, or angiostatin binding portion thereof.

2. The method of claim 1 wherein said angiostatin bears a detectable label.

Sub A2 3. The method of claim 1 wherein said ATP synthase, or angiostatin binding portion thereof, is attached to a solid support.

4. The method of claim 1 wherein said ATP synthase, or angiostatin binding portion thereof, is associated with a lipid membrane.

5. The method of claim 4 wherein said membrane is a membrane of an intact cell.

6. The method of claim 5 wherein said cell naturally expresses ATP synthase.

Sub A3 7. The method of claim 5 wherein said cell has been transformed with a nucleic acid sequence that encodes said ATP synthase, or angiostatin binding portion thereof.

8. A compound identified in the method of claim 1 as inhibiting the binding of angiostatin to said ATP synthase or angiostatin binding portion thereof.

9. A compound identified in the method of claim 1 as enhancing the binding of angiostatin to said ATP synthase or angiostatin binding portion thereof.

Sub A4 10. A method of screening a test compound for its ability to modulate a bioactivity resulting from binding of angiostatin to ATP synthase comprising:

i) contacting said test compound and angiostatin with a cell that expresses ATP synthase, or angiostatin binding portion thereof, under conditions such that angiostatin can bind to said ATP synthase, or angiostatin binding portion thereof, in the absence of said test compound, and

ii) determining the amount of angiostatin required to achieve the same bioactivity in the presence of said test compound as in the absence of said test compound,

wherein a reduction in the amount of angiostatin required to achieve said same bioactivity in the presence of said test compound indicates that said test compound is an angiostatin agonist, and

wherein an increase in the amount of angiostatin required to achieve said same bioactivity in the presence of said test compound indicates that said test compound is an angiostatin antagonist.

11. An angiostatin agonist identified in accordance with the method of claim 10.

12. An angiostatin antagonist identified in accordance with the method of claim 10.

Sub A5 13. The method of claim 10 wherein said bioactivity is inhibition of cell proliferation.

14. The method of claim 10 wherein said bioactivity is enhancement of proton pumping.

15. A method of inhibiting the angiogenesis inhibitory effect of angiostatin in a patient comprising

administering to said patient an amount of an angiostatin antagonist that binds an angiostatin binding portion of ATP synthase sufficient to effect said inhibition.

16. A method of inhibiting the angiogenesis inhibitory effect of angiostatin in a patient comprising administering to said patient an amount of a soluble angiostatin binding portion of ATP synthase sufficient to effect said inhibition.

17. A method of enhancing the angiogenesis inhibitory effect of angiostatin in a patient comprising administering to said patient an amount of an angiostatin agonist that binds to an angiostatin binding portion of ATP synthase sufficient to effect said enhancement.

18. An expression construct comprising a vector and a nucleic acid sequence encoding the α subunit of ATP synthase, or angiostatin binding portion thereof, operably linked to a promoter.

19. A host cell comprising the construct of claim 18.

20. A method of producing the α subunit of ATP synthase, or angiostatin binding portion thereof, comprising culturing the host cell of claim 19 under conditions such that said nucleic acid is expressed and said α subunit of ATP synthase, or angiostatin binding portion thereof, is thereby produced.

21. An antibody specific for the α subunit of ATP synthase, or angiostatin binding portion thereof, or antigen binding portion thereof.

22. A kit comprising ATP synthase, or angiostatin binding portion thereof, and angiostatin, or truncated form thereof.

23. An isolated complex comprising angiostatin and ATP synthase, or angiostatin binding portion thereof.

24. The complex according to claim 23 wherein said complex is bound to a solid support.